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Non-equilibrium phenomena and molecular reaction dynamics: mode space, energy space, and conformer space

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Abstract

The ability to characterize and control matter far away from equilibrium is a frontier challenge facing modern science. In this article, we sketch out a heuristic structure for thinking about different ways in which non-equilibrium phenomena can impact molecular reaction dynamics. Our analytical schema includes three different regimes, organized according to increasing dynamical resolution: at the lowest resolution, we have conformer phase space, at an intermediate resolution we have energy space, and at the highest resolution we have mode space. Within each regime, we discuss practical definitions of non-equilibrium phenomena, mostly in terms of the corresponding relaxation timescales. Using this analytical framework, we discuss some recent non-equilibrium reaction dynamics studies spanning isolated small-molecules, gas phase ensembles, and solution phase ensembles. This includes new results that provide insight into how non-equilibrium phenomena impact the solution phase alkene-hydroboration reaction. We emphasize that interesting non-equilibrium dynamical phenomena often occur when the relaxation timescales characterizing each regime are similar. In closing, we reflect on outstanding challenges and future research directions to guide our understanding of how non-equilibrium phenomena impact reaction dynamics.

Introduction

Understanding how physical processes far from equilibrium impact systems within physics, chemistry, and biology is a current ‘grand challenge’ facing 21st century science.¹ Indeed, many of the most commonly utilized physical laws invoked across a wide range of scientific applications are derived from equilibrium thermodynamics. Despite a well-developed mathematical apparatus for understanding equilibrium systems and our increasing ability to accurately predict the equilibrium properties of specific systems, most phenomena in the natural world occur in a non-equilibrium regime. It is often said that life is a non-equilibrium process, and this applies both to living organisms and the systems in which they are embedded: e.g., the delicately balanced reaction cycles that happen inside a cell, the firing of electrical impulses that cause our heart to beat, the formation and dissipation of perturbations within local and global weather systems, the time-evolution of social networks and stock markets, the spread of epidemics, etc.¹

Non-equilibrium phenomena may be observed at all levels at which matter is organized, from electron dynamics to cellular processes to star formation. With applications to chemistry, a substantial quantity of work has been done examining non-equilibrium phenomena imposed by boundary conditions and external fields.² However, the focus of this article is transient non-equilibrium phenomena within molecular reaction dynamics and kinetics – and in particular how such phenomena impact chemical reactions. The most commonly invoked models in the field of molecular reaction dynamics are dominated by references to free energies and transition state theory (TST), both of which have foundations in equilibrium thermodynamics. However, an increasing number of studies are revealing important non-equilibrium effects that cannot be captured by the standard equilibrium frameworks and which significantly impact chemical reactions. An exhaustive review citing all the work that has contributed to progress in non-equilibrium reactivity would require space far beyond what is available here and is not therefore possible. Rather, this article outlines an analytical schema divided into regimes that provide increasing dynamical resolution: conformer phase space, energy space, and mode space. These offer a useful organizational structure for thinking about different ways in which non-equilibrium phenomena can impact molecular reaction dynamics. Using this framework, we highlight a range of well-established and recent developments within reaction dynamics and kinetics, spanning isolated small-

molecule studies, gas phase studies, and liquid phase studies, including new results for the alkene-hydroboration reaction. At the close of this article, we reflect on challenges and future research directions.

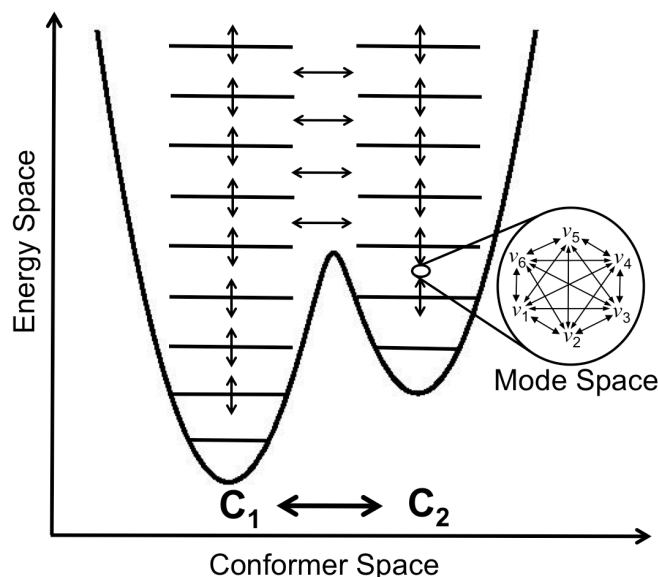


Figure 1: different regimes of non-equilibrium phenomena. At the lowest level of resolution, population may flow within *conformer phase space* between C_1 and C_2 . At an intermediate level of resolution, conformer phase space may be further partitioned to reveal different regions within molecular *energy space*. With higher resolution, energy space may be resolved into *mode space*, with energy flow amongst different molecular modes. The figure illustrates a kinetic network for flow of energy amongst a set of six molecular vibrations $v_1 - v_6$.

Identifying Non-Equilibrium Regimes

Conformer Phase Space

Figure 1 presents a useful schematic for thinking about different regimes of molecular non-equilibrium phenomena discussed in this article. The lowest level of resolution shown in Fig 1 concerns population flux that occurs as a molecular ensemble explores different regions of its available phase space on a single electronic potential energy surface (PES), indicated as a kinetic transformation wherein some conformer C_1 may interconvert to some conformer C_2 . From small molecules to proteins, this is perhaps the most common way in which chemists think about reactivity, and essentially amounts to distinguishing between ‘chemically significant’ changes in the coordinates, \mathbf{q} , used to represent molecular systems. In the limit of canonical equilibrium, p_i , the probability of finding the system in conformer i (e.g., $i = 1, 2$ in Fig 1) may be written as:

$$p_i(T) = \frac{Q_i(T)}{\sum_{i \in N} Q_i(T)} \quad (\text{E1})$$

where $Q_i(T)$ is the partition function for conformer i at some temperature T , and the summation is over all N conformers within the molecule's total phase space. 'Non-equilibrium' within conformer phase space refers to a situation where the ensemble populations of molecular conformers do not follow what we would expect on the basis of (E1).

Energy Space

A molecule's conformer phase space may be further resolved into microcanonical 'energy space'. Different regions within this space may be identified by the total (kinetic + potential) energy of the molecular system, a conserved quantity within both classical and quantum mechanics. Figure 1 represents this space as a set of discrete energy states along the y-axis. Population flow between different regions of energy space (represented by a set of vertical arrows) is facilitated by interactions with some sort of bath. The total energy of some molecular conformer i is typically described by some Hamiltonian function H , which may be expressed as a function of displacement within the modes of which the system is composed, or some other set of characteristic internal coordinates, \mathbf{q} . The energy-resolved picture may be linked to molecular phase space via the partition function of a particular molecular conformer as follows:

$$Q_i(T) = \int_{E=0}^{E=\infty} \rho_i(E) \exp(-\beta E) dE \quad (\text{E2})$$

where $\rho_i(E)$ is the density (or degeneracy) of states for conformer i at some energy E , and $\beta = (kT)^{-1}$. The corresponding probability of finding conformer i with a total energy E at some temperature T may be written as:

$$p_i(E) = \frac{\rho_i(E)}{Q_i(T)} \quad (\text{E3})$$

Within the energy space of conformer i , 'non-equilibrium' often refers to a situation in which the energy distribution function $p_i(E)$ does not follow what we would expect based on (E3).

Mode Space

Microcanonical energy space is composed of a set of microstates, each of which has a particular energy E . For small and medium sized molecules at low energies, there are usually only a few such microstates; however, the density of states increases rapidly with energy. Any given microstate may be distinguished from any other microstate by resolving the constituent modes whose combination makes up a particular microstate. These modes may represent any of a number of types of molecular motion including normal mode vibrations, local mode vibrations, librations, etc. While the choice of framework for describing the modes depends on the system under investigation, the important point is that there is some set of molecular motions (i.e., modes) whose combinations result in a set of microstates. This level of resolution we refer to as ‘mode space’. One of the utilities of the mode space perspective is that it easily allows us to identify and analyze the specific microscopic motions characterizing a molecule’s dynamics. Fig 1 shows a schematic for population flow between six different vibrational modes ($\nu_1 - \nu_6$) using a simple kinetic scheme where the arrows represent some different pathways that energy may take. For a polyatomic molecule with a total energy E , there are usually a number of different states with energy E . Each state corresponds to a different way of partitioning the available molecular energy amongst all the different modes (the number of modes goes as $3n - 6$ where n is the number of atoms in the molecule). Within the ergodic limit, the assumption is that intramolecular energy transfer between modes is rapid, and every state is equally likely. Statistically, for a molecule with S states that have a total energy E , we may calculate $\langle E_j \rangle_E$, the average energy in a particular mode j at some total molecular energy E , as follows:

$$\langle E_j \rangle_E = \frac{1}{S} \sum_{k=1}^S E_{j,k} \quad (\text{E4})$$

where k runs over all S states with a total molecular energy E , and $E_{j,k}$ is the energy within mode j for state k . Summing over the average energy in each mode then recovers the total molecular energy – i.e.:

$$\sum_{j=1}^{3n-6} \langle E_j \rangle_E = E \quad (\text{E5})$$

Mode space is amongst the most fundamental perspectives from which to analyze molecular behavior, since it relates to the fundamental motions that drive chemical change. Within mode space, non-equilibrium often refers to circumstances in which the energy content in some mode differs substantially from what we would expect based on (E4). Indeed, such perturbations and corresponding localization of significant energy in some small subset of

modes is often a prerequisite for any molecule to undergo reactive change.³ This leads us to an important point: all of chemical reactivity fundamentally depends on how molecules shuffle energy between modes.

Population Flux in Conformer Space, Energy Space, and Mode Space

(E1) – (E5) provide a useful lens for resolving different regimes of non-equilibrium phenomena within molecules. In the simplest limit, *non-equilibrium systems are characterized by population distributions that deviate from what we would expect in the equilibrium ensemble limit*. More detailed analyses are able to reveal the microscopic physical mechanisms responsible for these deviations and the corresponding pathways by which non-equilibrium systems relax to equilibrium. It is important to note that statistical mechanics not only provides frameworks for calculating populations in equilibrium systems; it also allows us to calculate population flux within equilibrium systems. For example, at canonical equilibrium, where it is appropriate to invoke free energy descriptions, rate coefficients describing flux between different regions of conformer phase space may be estimated using transition state theory (TST):

$$k(T) = \Gamma(T) \frac{kT}{h} \frac{Q_{TS}}{Q_R} \exp(-\beta E_0) \quad (\text{E6})$$

where Q_{TS} and Q_R are the respective transition state (TS) and reactant (R) partition functions, E_0 is the potential energy of the transition state with respect to that of the reactant, and $\Gamma(T)$ is a coefficient which accounts for both in the effect of both quantum tunnelling and recrossing due to friction.⁴ At microcanonical equilibrium, Rice-Ramsperger-Kassel-Marcus (RRKM) theory provides a similar description of the rate coefficient for population transfer between different regions of conformer phase space:

$$k(E) = \frac{\int_{E_0}^E \rho_{TS}(E) dE}{h \rho_R(E)} \quad (\text{E7})$$

where $\rho_{TS}(E)$ and $\rho_R(E)$ are the respective densities of states for the transition state and reactant. Within mode space, intramolecular vibrational energy redistribution (IVR) for larger polyatomic molecules is typically expressed in terms of Fermi's golden rule as follows:^{5,6}

$$k_{i \rightarrow j} = (2\pi / \hbar) |\langle j | H | i \rangle|^2 \delta(E_i - E_f) \quad (\text{E8})$$

where $k_{i \rightarrow j}$ is the rate coefficient for energy transfer from mode i to mode j , $\langle j | H | i \rangle$ is the corresponding mode-mode matrix coupling element, and E_i, E_j are the energies of states i and j . The total rate coefficient for energy flow out of a particular mode requires summing over all possible j acceptor modes in (E8). The availability of frameworks like (E6 – E8) for calculating population flux across the regimes shown in Fig 1 highlights an additional criterion for identifying non-equilibrium phenomena: namely, *cases in which the rate of population transfer differs substantially from what we would predict using equilibrium frameworks – e.g., TST, RRKM theory, or Fermi’s golden rule.*

Relaxation Timescales

The partitioning shown in Fig 1 is partially motivated by the fact that each regime tends to have its own characteristic timescale, τ^{eq} , on which perturbations relax to equilibrium, with the most common assumption that $\tau_{mode\ space}^{eq} \ll \tau_{energy\ space}^{eq} \ll \tau_{configuration\ space}^{eq}$. However, it is important to note that several of the most interesting non-equilibrium molecular phenomena (including the examples discussed below) concern cases wherein $\tau_{mode\ space}^{eq}$, $\tau_{energy\ space}^{eq}$, and $\tau_{configuration\ space}^{eq}$ are competitive.

Specification of characteristic relaxation timescales is an important basis for developing Markov models of chemical dynamics,⁷ which rely on the assumption that memory effects within a dynamical system need not be considered. Hence, evolution from time t to $t + \Delta t$ depends only on a system’s state at time t , irrespective of its state at time $t - \Delta t$. Insofar as (E6) – (E8) only require knowledge of the system at time t , they are all built on this assumption.

On a small enough timescale, classical and quantum mechanics specify that the time evolution of any system from $t - \Delta t \rightarrow t \rightarrow t + \Delta t$ is entirely deterministic, so that different time dependent states are highly correlated. Given this fact, the ubiquity of Markov models in describing dynamical ensembles may come as a bit of surprise. The key is a judicious definition of the magnitude of Δt . For complex systems with coupled degrees of freedom, it is generally possible to find values of Δt where dynamical properties measured at $t + \Delta t$ have decorrelated from those measured at time t .⁸ Quantitatively, we may define Δt as the timescale required for an ensemble averaged time-correlation function to decay to zero.

Each of the regimes shown in Figure 1 has a characteristic decorrelation timescale, leading us to another useful criterion for identifying circumstances during which molecular

systems are not likely to be in equilibrium with respect to some initial perturbation: namely, *at times shorter than the decorrelation timescale, i.e. when $\Delta t < \tau^{eq}$.*

Non-Equilibrium Effects in Chemistry

Isolated small molecule dynamics and kinetics

For isolated systems within the gas phase, studies on small molecule systems have shown that chemical reactions and molecular dynamics often occur in a regime which is far from equilibrium. Early observations made on $A + BC$ reactions were synthesized by Polanyi, who observed that PES topologies govern the extent to which products are produced in excited non-equilibrium quantum state distributions.⁹ The qualitative rules he introduced for predicting non-equilibrium product distributions come from recognizing that reaction outcomes can be rationalized using a system's trajectory. Trajectory-based models have since become a staple within chemical dynamics, and sophisticated theoretical models built on both classical and quantum mechanics are able to reliably rationalize and predict non-equilibrium outcomes of small molecule experiments.¹⁰

Recognizing that chemical reactions produce excited products raises an interesting question if one considers the reverse direction – i.e., is it possible to control chemistry by selectively exciting modes that are strongly coupled to the reaction coordinate?^{11,12} For small molecules the answer certainly appears to be affirmative.^{13,14} For example, Crim and co-workers examined the $H + HOD$ reaction, and showed that vibrational excitation of the $H-OD$ stretch led to $H_2 + OD$ products, while excitation of the $HO-D$ stretch led to $OH + HD$ products.¹⁴ For larger polyatomics efforts to control chemistry using mode selective excitation is significantly more complicated owing to the fact that IVR is extremely rapid,^{5,15} with the result that initially localized energy can quickly flows into other molecular modes, where it is little more useful than heat in driving a chemical reaction.¹² Despite these challenges, considerable advances have been made controlling chemical reactions using exquisitely tailored ultrafast optical pulses, both experimentally and theoretically.¹⁶

In the thermal regime, a number of recent theoretical and experimental studies have highlighted polyatomic systems in which the outcomes of chemical reactions, as reflected in the relative product yields, are very different than one would predict using the equilibrium frameworks discussed above.¹⁷⁻²⁰ Recent work has highlighted a number of systems in which the observed reaction rates are faster than would be predicted based on equilibrium statistical

mechanics.²⁰ In general, these observations arise because $\tau_{mode\ space}^{eq}$ is similar to $\tau_{configuration\ space}^{eq}$. In a number of these systems, it is possible to rationalize the non-equilibrium behavior according to the structure of the underlying PES governing atomic rearrangement. For example, the assumed separation in equilibrium timescales often breaks down in the neighborhood of valley-ridge inflection points.¹⁹ These sorts of PES topologies often give rise to largely ballistic dynamics with long decorrelation timescales in mode space. This allows the system to traverse chemically distinct regions of the conformer phase space in relatively short times on the order of a few molecular vibrations. In such cases, Markov models generally provide a poor description of the rates for transfer between different regions of molecular phase space. Other well-known circumstances in which $\tau_{mode\ space}^{eq} \sim \tau_{configuration\ space}^{eq}$ include cases where energy is localized in a particular mode or subset of modes that are spectrally distinct from and only weakly coupled to other modes in the system.^{17,21}

Gas-Phase Dynamics and Kinetics

Gas phase chemical reactions are usually embedded in an ensemble of weakly interacting collision partners. In these cases, we can distinguish the system from the bath as follows: the system contains the molecule(s) undergoing the chemical reaction of interest, and the bath contains the ensemble of inert collision partners that exchange energy with the system through inelastic collision processes. This is effectively the picture described by the simple mechanism shown below:



where A and B are bimolecular reactants that form AB*, an encounter complex with a non-equilibrium distribution in energy space. AB* has one of two fates: it may undergo (1) fast dissociation back to A + B, or (2) a series of weak collisions with the bath gas M that ultimately stabilize it to AB.²²

The R1a/R1b kinetic scheme qualitatively encapsulates one of the most ubiquitous manifestations of non-equilibrium phenomena within energy space – namely fall-off curves, in which experimental association rate coefficients show strong non-linear dependences on pressure.²³ To understand these observations, there are two important limits to consider:

- (1) At low pressures, the phenomenological rate coefficient for A + B association is small because redissociation to A + B dominates. This arises because $\tau_{energy\ space}^{eq}$ (the timescale for relaxation of AB* to AB) is competitive with $\tau_{configuration\ space}^{eq}$. In this limit, the system closely follows the RRKM model of (E7).
- (2) At high pressures, collisions with bath molecules quickly relax AB* to AB, and $\tau_{energy\ space}^{eq} \ll \tau_{configuration\ space}^{eq}$. This decreases the probability of dissociation, increasing the phenomenological association rate coefficient. In this limit, free-energy descriptions are appropriate, and the system closely follows canonical TST specified in (E6).

At terrestrial temperatures and pressures, many important chemical reactions take place in an intermediate pressure regime where $\tau_{energy\ space}^{eq}$ is similar to $\tau_{configuration\ space}^{eq}$.²⁴⁻²⁶ For example, recent work investigating atmospheric association reactions to form peroxy radicals clearly shows that O₂ “intercepts” vibrationally hot addition complexes.²⁷ As shown in Fig 2, association of OH + acetylene in the atmosphere (298K, 760 torr) forms beta-hydroxy-vinyl (BHV) isomers with a strongly non-equilibrium energy distribution. In Fig 2, these are denoted CT** and CC**. At times less than 630 ps, relaxation within energy space is minimal, and the CT** to CC** ratio is 1:1. Full relaxation within both energy and conformer phase space are complete (blue curve) at times longer than 20 ns, and the equilibrium CT:CC ratio is 78:22. In between the short and long time limits, the BHV isomers are in an intermediate state of relaxation, a state denoted in Fig 2 as CT* and CC* (red curve). This matters because the different BHV isomers lead to different products, with CT + O₂ giving glyoxal + OH products, and CC + O₂ giving formic acid + HCO products. The atmospheric OH yield (298K, 760 torr) reflects the fact that O₂ ‘intercepts’ ~25% of CT* and CC* prior to relaxation to CT and CC. More generic analysis indicates that O₂ is capable of “intercepting” a range of different organic radicals prior to their relaxation in the atmosphere,^{27,28} revealing atmospheric bimolecular reactions as a new area in which non-equilibrium effects matter.

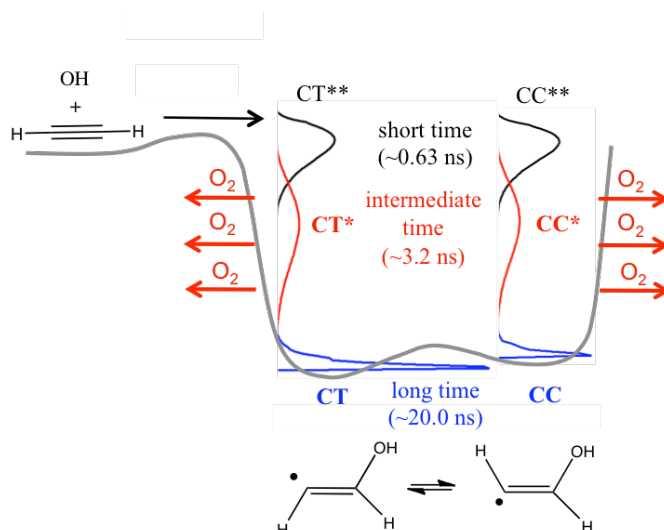


Figure 2: Illustration of how O_2 “intercepts” vibrationally hot addition complexes in the atmosphere.²⁷ OH + acetylene association forms two different vibrationally hot BHV isomers: CT** and CC**, both of which have a fast equilibrium. At times less than 0.63 ns (black curve), little relaxation occurs and the CT**:CC** ratio is 1:1. By ~20 ns, relaxation is complete (blue curve), and the thermal 298K CT:CC ratio is 78:22. Under atmospheric conditions, O_2 efficiently intercepts the BHV isomers at range of energies over an intermediate state of relaxation, denoted CT* and CC*.

A useful framework for quantitative analysis of competition between energy space relaxation and conformer phase space population flux is provided in the form of the energy grained master equation (EGME).^{22,25,29} The EGME is a Markov state model that describes population evolution within a set of energy-resolved regions of conformer phase space. On the assumption that relaxation within mode space is fast and the system is ergodic, the EGME partitions different regions of conformer space into different energy states (or ‘grains’), as shown in Figure 1. Population flux between grains are then modeled as follows:

- (1) Amongst energy grains of the same energy, transitions between different regions of conformer phase space are modeled using (E7).
- (2) Amongst grains of different energy within the same region of conformer phase space, upward and downward transitions are modeled by combining collision theory with a function describing the probability that any given collision transfers some quantity of energy.

Fundamental questions remain regarding the appropriate form for the energy transfer functions used in the EGME. Nevertheless, its achievements are impressive, and it has been successfully utilized to rationalize and predict large quantities of experimental data spanning a range of conditions that includes both adiabatic and (more recently) non-adiabatic kinetics.³⁰

Solution phase dynamics and kinetics

With developments in experimental methods, computational resources, and theoretical frameworks, an increasingly studied aspect of non-equilibrium dynamics concerns chemical reactions in liquids.^{5,31,32} The system/bath partition in such systems is naturally defined with reference to the solute and solvent. At atmospheric temperatures and pressure, for example, a cubic box with a side length of 34.4 Å contains an average of one molecule. For typical organic solvents, the same sized box contains hundreds of molecules. Understanding non-equilibrium reaction phenomena in liquids is complicated because: (1) the densely packed solvent environment can substantially modify the solute PES with consequences for population flux between different regions of conformer phase space;⁵ (2) ‘crowding’ substantially impacts molecular motion with knock-on effects for dynamics;^{3,33} (3) the dynamically significant fractions of both mode and energy space expand considerably owing to the close proximity of solvent molecules and crowding.

A number of experimental and theoretical studies have provided insight into relaxation dynamics and unimolecular dissociation following relatively high-energy photo-excitation pulses.^{33,34} But far fewer studies have been designed to examine non-equilibrium relaxation that follows in the wake of thermal reactions in solution.³⁵ Hence, it is commonly assumed that $\tau_{energy\ space}^{eq}$ and $\tau_{mode\ space}^{eq}$ are rapid enough for non-equilibrium effects to be negligible.³⁶ However, recent work aimed at developing a microscopic picture of non-equilibrium dynamics in solution phase reactions suggests otherwise. For example, recent studies examining thermal bimolecular reactions of CN with both cyclohexane and THF in a range of organic solvents have shown significant vibrational excitation in the nascent HCN products.^{3,31,37-39} One of several interesting new insights from this work has been the direct observation of two distinct post-reaction non-equilibrium relaxation timescales within energy space.^{3,39} The first relaxation timescale (panel A of Fig 3) follows in the immediate wake of the reaction, when the nascent HCN is in close proximity to its cyclohexyl co-product, and strong interaction between co-products facilitates rapid energy transfer and correspondingly fast HCN relaxation. The second relaxation timescale (panel B of Fig 3) occurs once HCN and cyclohexyl have diffused away from one another and into the bulk solvent. HCN relaxation is considerably slower following diffusion, owing to weaker interactions between HCN and the CH₂Cl₂ solvent. Beyond being an interesting observation, these two-timescale relaxation dynamics actually have a non-trivial impact on the interpretation of the experimental data: neglecting the fact that there are two different relaxation timescales leads to underestimation of the fraction of vibrationally hot HCN produced in the immediate

aftermath of the $\text{CN} + \text{C}_6\text{H}_{12}$ abstraction reaction.³ Related time-resolved studies of HCN produced from reaction of $\text{CN} + \text{THF}$ in THF solvent similarly show reveal two relaxation timescales, but their separation is rather less dramatic.³⁸

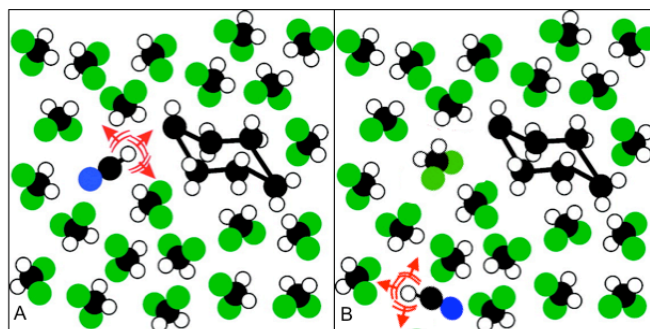
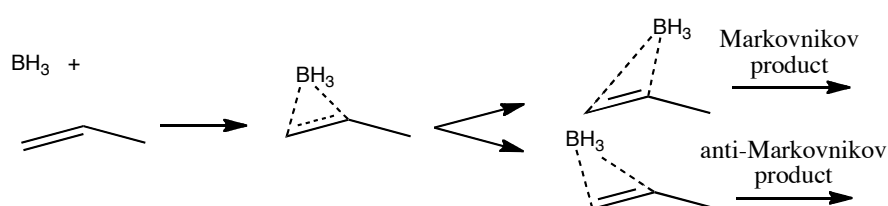


Figure 3: Illustration of the two different HCN relaxation timescales that follow in the wake of a bimolecular reaction wherein CN abstracts a hydrogen from C_6H_{12} . Panel A shows the fast relaxation regime, where HCN and C_6H_{11} are in close proximity immediately following abstraction. Panel B shows the slow relaxation regime, where the co-products have diffused away from one another.

Given this strong evidence of non-equilibrium phenomena in thermal bimolecular reactions, it is worth considering whether such effects impact chemical reactions. For a growing set of systems, recent work has identified solution-phase organic reactions in which non-equilibrium relaxation phenomena directly impact product yields.^{40,41} For example, it was recently shown that the relative yields of Markovnikov vs. anti-Markovnikov products in the well-known alkene hydroboration reaction are well described by EGME models of the sort discussed above. The relevant reaction scheme is as follows:



The key to the product partitioning concerns the nascent BH_3 –alkene complex (shown in Fig 4 embedded in a tetrahydrofuran (THF) solvent) which initially has a strongly non-equilibrium distribution in energy space with $\sim 46 \text{ kJ mol}^{-1}$ excess energy. As equilibrium sets in, anti-Markovnikov product formation increasingly dominates. EGME analysis suggests that the experimental product yields⁴² arise from the BH_3 –alkene complex having an intermediate energy distribution, somewhere between the equilibrium and strongly non-equilibrium limits, with owing to the fact that $\tau_{\text{energy space}}^{\text{eq}}$ and $\tau_{\text{configuration space}}^{\text{eq}}$ are very similar.

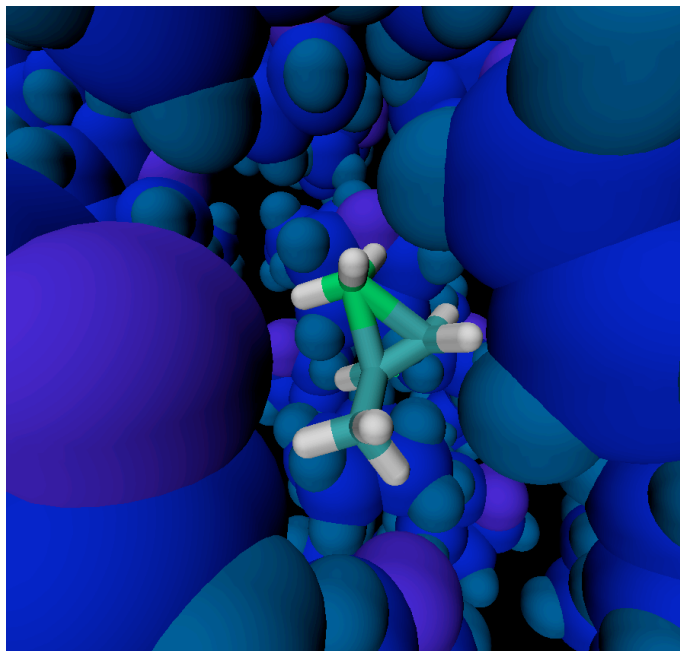


Figure 4: MD snapshot of the BH₃-alkene complex embedded in a THF solvent

To explain the experimental results, EGME calculations performed on the BH₃-alkene complex using a binary collision model required minimum energy relaxation rates on the order of 25 kJ mol⁻¹ ps⁻¹.⁴¹ To provide further microscopic insight into the origin of these values, we carried out solution phase MD modeling of the BH₃-alkene complex embedded in an explicit solvent (a snapshot is shown in Fig 4). These calculations were carried out using the TINKER MD package along with the MM3 force field modified to include five-fold coordinated Carbon and Boron, as well as bonding, angle, and dihedral terms for modeling the interaction between BH₃ and propene. Parameters for the additional molecular mechanics terms were adjusted to give a set of vibrational frequencies for the BH₃-alkene complex which agreed with B3LYP/6-31G(2df,p) calculated frequencies to better than 12%. To monitor energy dissipation in the BH₃-alkene complex, we constructed time-averaged internal energy correlation functions as follows:

$$C(t) = \left\langle 2KE_{avg}(0) \cdot 2KE_{avg}(t) \right\rangle - \left\langle 2KE_{avg}(t) \right\rangle^2 \quad (\text{E9})$$

where the angled brackets indicate an average over the entire ensemble, $KE_{avg}(t)$ is the total kinetic energy of the BH₃-alkene complex at time t averaged over 0.5 ps time windows, and KE_{avg}^{eq} is the equilibrium average of the kinetic energy in the complex, again averaged over 0.5 ps time windows. The values required in (E9) were obtained from analyzing 5 ns of MD simulations, which were sufficient to achieve convergence in the correlation functions. In the limit of a purely harmonic potential, the virial theorem states that the time averaged kinetic

energy is equal to the time averaged potential energy. For the preliminary results reported herein, we calculated an approximation to this harmonic virial limit, simply treating the total internal energy of the complex as $2KE_{avg}$. We anticipate that the most significant errors in this approach arise from neglecting to project out translational and rotational motion. But based on equilibrium statistical mechanics and previous work,³⁹ these components should contribute no more than 15% percent to the total kinetic energy of the complex. Using linear response theory (LRT)⁴³ along with the (E9) correlation functions, we calculated time-dependent decays of excess internal energy within the BH_3 -alkene complex, $E_{complex}(t) - \langle E_{complex} \rangle$, as follows:

$$E_{complex}(t) - \langle E_{complex} \rangle = \frac{C(t)}{C(0)} [E_{complex}(0) - \langle E_{complex} \rangle] \quad (\text{E10})$$

Fig 5 shows results obtained by setting the initial excess internal energy within the complex, $E_{complex}(0) - \langle E_{complex} \rangle$, to 46 kJ mol^{-1} . The results give an average energy decay rate of $\sim 3.5 \text{ kJ mol}^{-1} \text{ ps}^{-1}$ (obtained from a single exponential fit). These results are broadly consistent with the EGME results; however, further work is required to explore: (1) the physical origin of the short-time deviations from a single exponential decay shown in Fig 5; (2) the extent to which more accurate treatments of the solvent-solute force field impact the vibrational energy relaxation rate (previously shown to be important with THF as a solvent³⁸), and (2) how the correlation function relaxation profile in energy space relates to non-equilibrium population flux within mode space.

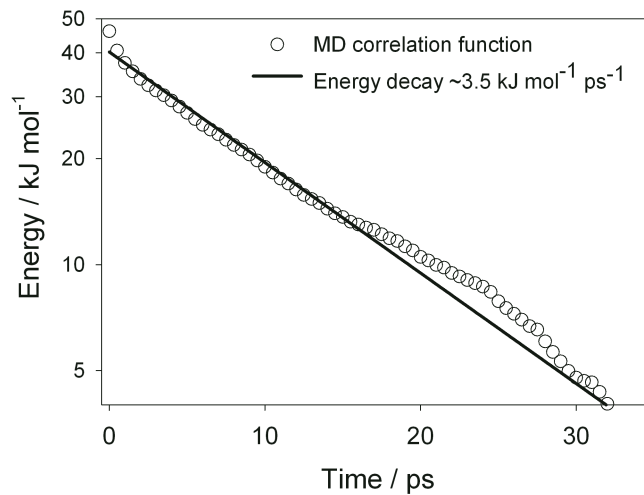


Figure 5: time dependent internal energy of the BH_3 -alkene complex embedded in a THF solvent, calculated using (E9) – (E10). The initial excess energy in the complex is 46 kJ mol^{-1} .

Conclusions and Challenges

Non-equilibrium phenomena are the subject of increasing attention within the physical sciences. This article outlines a heuristic organizational framework for thinking about non-equilibrium phenomena as they relate to adiabatic chemical reaction dynamics. The framework partitions non-equilibrium phenomena based on relaxation timescales in mode space, energy space, and conformer phase space. While we believe this schema to be useful, it is important to point out the following: within molecules, it is often the case that each of these domains couple to one another – i.e., mode space dynamics affect the dynamics within energy space, and both subsequently impact dynamics within conformer phase space. In general, many of the most interesting non-equilibrium cases occur when relaxation timescales within these regimes are similar, and this article highlights a number of such cases.

Our understanding of adiabatic non-equilibrium phenomena in isolated small molecules is relatively advanced compared to other fields, and has led to the development of sophisticated theoretical models that are able to predict and explain a range of experimental results.⁴⁴ Significant challenges in the small-molecule field remain – for example, in understanding non-adiabatic dynamics and testing efficient approaches for obtaining accurate PESs. Nevertheless, successes in understanding non-equilibrium dynamics in small molecules have paved the way for us to tackle increasingly complex systems with some degree of confidence. Regarding our understanding of how non-equilibrium phenomena impact simple elementary reactions within gases, progress has also been made; however, a number of questions remain, and we continue to uncover surprises.^{26,27} For example, our fundamental understanding of the appropriate form for generic energy transfer models remains lacking,⁴⁵ particularly for the relaxation of molecules with significant vibrational excitation in regimes where dynamics are significantly anharmonic. Additionally, the extent to which non-equilibrium phenomena impact chemical reactions in coupled kinetic networks (e.g., in the atmosphere) remains an exciting question.

Growing evidence suggests non-equilibrium phenomena impact a range of chemical reactions within liquids in a manner that cannot be captured using simple free energy pictures and canonical TST; however, many open questions remain. Similar to the gas phase, there is a lack of fundamental understanding regarding generic functional forms able to describe solute/solvent energy transfer in both energy and mode space.⁴⁶ Developing multi-dimensional “maps” of mode specific energy transfer pathways during chemical reactions would go some way to helping us to visualize relaxation processes and develop our

fundamental understanding of energy flow during the course of a chemical reaction. This will provide insight into IVR processes, solvent-solute interactions, and solvent crowding effects (e.g., friction). Just like in the small molecule field, an important challenge involves developing generic and efficient approaches for evaluating the solvent/solute PES. Detailed experiments and dynamics simulations will enable progress here. Ultimately, the aim is coarse-grained transferable models with predictive power.

Beyond liquids, biochemical reactions offer exciting territory for investigating non-equilibrium phenomena. For small peptides, studies of reaction and folding dynamics have highlighted cases where non-equilibrium phenomena significantly impact population flux within different regions of conformer phase space.⁴⁷ Detailed studies of how biomolecules relax in mode and energy space are challenging owing to biomolecular heterogeneity, size and natural variability.⁴⁸ Nevertheless, it will be fascinating to explore whether studies carried out along these lines⁴⁹ lead to the development of transferable physical models that provide insight into how living systems manage microscopic non-equilibrium phenomena.

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